

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:) Art Unit: 1627
LADNER, et al.) Examiner: CELSA, Bennett
Serial No.: 09/896,095) Confirmation No. 8870
Filed: June 29, 2001) Washington, D.C.
For: DIRECTED EVOLUTION) August 28, 2002
OF NOVEL BINDING PROTEINS) Docket No.: LADNER=7L



Commissioner of Patents
Washington, D.C. 20231

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SECOND PRELIMINARY AMENDMENT

Sir:

Prior to action on the merits, please enter the following amendments and remarks:

IN THE CLAIMS

Please add the following new claims:

101. (New) A non-naturally occurring or purified protein which inhibits human neutrophil elastase, and which is a protein comprising a mutant Kunitz domain, said domain being characterized by Cys at positions corresponding to bovine pancreatic trypsin inhibitor (BPTI) position 12, and Phe at a position corresponding to BPTI 33;

where, in said mutant Kunitz domain, the residue corresponding to BPTI position 18 is Phe, and

the residue corresponding to BPTI position 39 is selected from the group consisting of Met, Lys, Trp, Arg, His, Leu, or Glu;

the residue corresponding to BPTI position 40 is Ala or Gly; and

the residue corresponding to BPTI position 41 is Lys, Glu, Gln, Asp, His, Asn or Tyr; and

the residues corresponding to BPTI position 39-42 are not Arg-Ala-Lys-Arg.

101. (New) The protein of claim 101 in which the residues corresponding to BPTI positions 14 and 38 are Cys, and the residue corresponding to BPTI position 37 is Gly; and

the residue corresponding to BPTI position 45 is Phe and the residue corresponding to BPTI position 43 is Asn.

103. (New) The protein of claim 101 in which the residue corresponding to BPTI position 42 is Gly.

104. (New) The protein of claim 102 in which the residue corresponding to BPTI position 42 is Gly.

105. (New) The protein of claim 101 where the residues corresponding to BPTI positions 39-42 are not Met-Gly-Asn-Gly.

106. (New) The protein of claim 102 where the residues corresponding to BPTI positions 39-42 are not Met-Gly-Asn-Gly.

107. (New) The protein of claim 104 where the residues corresponding to BPTI positions 39-42 are not Met-Gly-Asn-Gly.

108. (New) The protein of claim 101 which the residue corresponding to BPTI position 42 is selected from the group consisting of Arg, Ala, Gly, Ser, Glu, His, Asn, Met, Asp, Lys, Glu and Leu.

109. (New) The protein of claim 101 which has a binding affinity for human neutrophil elastase in the range of 100 pm to 1 pm.

110. (New) The protein of claim 101 which comprises the amino acid sequence of a protein selected from the group consisting of EpiNE7.1-7.40.